INTERNATIONAL SEARCH REPORT

International Application PCT/US 91/00245

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [5]

According to International Patent Classification (IPC) or to both National Classification and IPC

see attached sheet

II. FIELDS SEARCHED

Minimum Documentation Searched [6]

Classification System	Classification Symbols
see attached sheet	

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [7]

see attached sheet

III. DOCUMENTS CONSIDERED TO BE RELEVANT [14]

Category [8]	Citation of Document, [16] with indication, where appropriate, of the relevant passages [17]	Relevant to Claim No. [18]
see attached sheet		

[8] Special categories of cited documents: [15]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search [3]	Date of Mailing of this International Search Report [3]
14 MARCH 1991	26 APR 1991
International Searching Authority [1]	Signature of Authorized Officer [19]
ISA/US	GABRIELLE E. BIGAISKI

Form PCT/ISA/210 (second sheet) (May 1986)

#11

U.S. Serial No. 08/112,848
Attorney Docket No. 24364-20002.23

PCT/US/ 91/00245
Attachment to Form PCT/ISA/210
I. Classification of subject matter
IPC(5): C12P 21/06; C12N 15/00
U.S. Cl.: 435/69.1, 172.3; 800/2

II. Fields searched
U.S. Cl. 435/69.1, 69.6, 70.1, 172.3; 436/547; 530/387; 800/2; 935/22, 65, 106

Databases: Dialog Information Services Online (File sets Medline and World Patent Index)
Automated Patent System (File USPAT)

gene transfer or gene replacement or gene inactivation, homologous recombination; embryonic stem cell, animal stem cell, embryonal carcinoma, transgenic animal or mammal, xenogeneic antibody or antiserum or immune response, immunoglobulin; immunoglobulin gene.

Attachment to Telephone Memorandum
PCT/US91/00245

Observations where unity of invention is lacking

Detailed reasons for holding lack of Unity of Invention.

There are three groups of claims: Group I is a method for producing antisera; transgenic animals; Group II is for embryonic stem cells. Group I is related as first mentioned product and process of use. Group II consists of a second mentioned product, which can exist independently of the first mentioned product. PCT Rules 13.1 and 13.2 do not provide for multiple products.

Itemized summary of claims groupings

I. Claims 1-7, drawn to a method for producing xenogeneic antisera, classified in Class 435, subclass 69.1.

Claims 8-18, drawn to transgenic animals with lesions in endogenous immunoglobulin genes, so that they can only express human immunoglobulin genes, classified in Class 800, subclass 2.

II. Claims 19-25, drawn to embryonic stem cells with lesions in endogenous immunoglobulin genes, classified in Class 435, subclass 230.1.

III. Documents considered relevant

Category	Citation	Claims
Y, P	US, A. 4,959,313 (TAKETO) 25 September, 1990 see entire document.	19-25
Y, P	US, A. 4,950,599 (BERTLING) 21 August, 1990 see entire document.	8-25
Y	Proc. Natl. Acad. Sci., USA. Vol. 83, issued April 1986, K.-I. Yamamura, et al., "Cell-type-specific and regulated expression of a human γ1 heavy-chain immunoglobulin gene in transgenic mice", pages 2152-2156, see entire document.	1-25
Y	Proc. Natl. Acad. Sci., USA. Vol. 86, issued November 1989, B. Koller, et al., "Inactivating the β2-microglobulin gene in mouse embryonic stem cells by homologous recombination", pages 8932-8935, see entire document.	1-25
A	Proc. Natl. Acad. Sci., USA. Vol. 83, issued July 1966, D. Ayares, et al., "Sequence homology requirements for intermolecular recombination in mammalian cells", pages 5199-5203, see entire document.	8-25
A	Proc. Natl. Acad. Sci., USA. Vol. 85, issued February 1988, R. Brinster, et al., "Introns increase transcriptional efficiency in transgenic mice", pages 836-840, see entire document.	1-25
Y	Prog. Nucleic Acid Res. Mol. Biol., Vol 36, issued 1989, R. Kucherlapalati, "Homologous recombination in mammalian somatic cells", pages 301-310, see entire document.	1-25
Y	Proc. Natl. Acad. Sci., USA. Vol. 86, issued October 1989, A. Shimizu, et al., "Immunoglobulin double-isotype expression by trans-mRNA in a human immunoglobulin transgenic mouse", pages 8020-8023, see entire document.	1-25